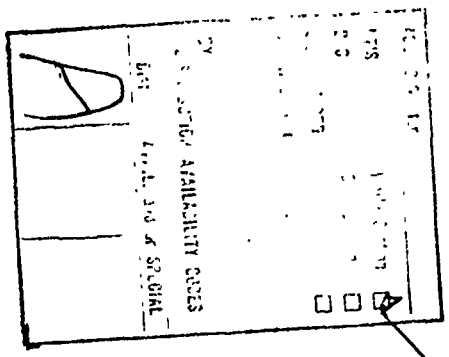
PORCINE BURN SHOCK - DEVELOPMENT OF A RELIABLE MODEL AND RESPONSE TO SODIUM, WATER, AND PLASMA LOADS ADMINISTERED FOR RESUSCITATION

Thomas L. Wachtel, et al

Army Aeromedical Research Laboratory
Fort Rucker, Alabama

June 1973



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PORCINE BURN SHOCK

Development of a Reliable Model and Response to Sodium, Water, and Plasma Loads Administered for Resuscitation

By

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June 1973

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Fort Rucker, Alabama 36360

U.S. Army Medical Research and Development Command

The Vivarium of the United States Army Aeromedical Research Laboratory is fully accredited by the American Association for Accreditation of Laboratory Animal Care.

In conducting this research, the investigators adhered to the "Guide for Laboratory Animals Facilities and Care" prepared by the Committee on the Guide for Laboratory Animals Facilities and Care, National Academy of Sciences, National Research Council. Humane procedures were utilized throughout, and a graduate veterinarian was in constant attendance to perform all surgical procedures and to ensure that all animals were fully anesthetized and insensitive to pain.

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ABSTRACT

Miniature swine are a sensitive and responsive animal for the study of burn shock resuscitation. The sodium loads requisite for resuscitation of burned swine can exert roughly the same effects when administered in volumes of from 25% to 50% less than those commonly employed clinically. Sodium excretion is more dependent upon the sodium load than upon the concentration of the saline solution. Plasma administration had no demonstrable resuscitative effect over and above that provided by the sodium and volume given in this model.

APPROVED: ROBERT W. BAILEY
Colonel, MSC
Commanding

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INTRODUCTION

New techniques in postburn fluid management have again raised the controversy over the relative value of sodium ion, fluid volume, and colloid in burn shock resuscitation.[1] Recent evidence has elucidated some of these factors,[2] but many of the subtleties in resuscitation remain unanswered. In addition, criticism has been raised as to the choice of an animal model for solving some of these problems, i.e., dog, rat, mouse, large non-human primates, etc. The pig has many factors mitigating in favor of its use as a burn shock model. This report develops the miniature swine as that model and shows its response to certain fluid regimens now in popular use.

METHODS AND MATERIALS

Thirty-three (33) white Minipigs* were procured, quarantined, freed of internal and external parasites, and verified to be healthy prior to use in this study.

Each animal was splenectomized to prevent autotransfusion.[3] When the animal had stabilized for two weeks or longer, central venous and arterial catheters were implanted.[4] Stainless steel electrodes were placed in each limb for electrocardiograph (ECG) monitoring. A suprapubic cystostomy catheter was employed. The animal was allowed to recover and stabilize for 48 hours. Baseline data (See Equipment List in Appendix A) were obtained in each awake, unrestrained pig (Figure 1).

The miniature swine were then fasted overnight, premedicated with

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*Modified Pitman Moore Strain of Miniature Swine, Vita Vet Laboratories, Marion, IN 39052

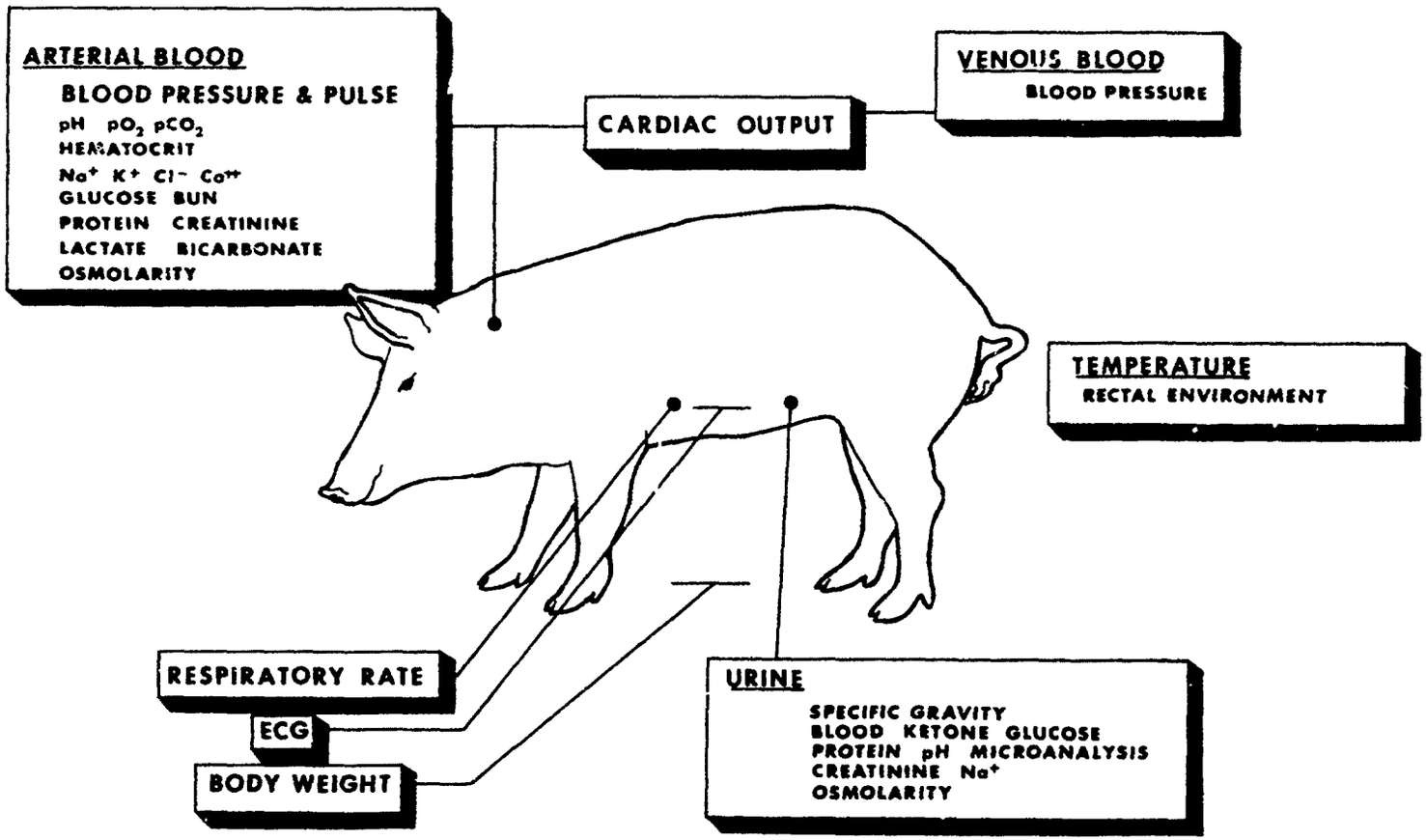

FIGURE 1. Data Acquisition System (See Equipment List)

Atropine (0.02 mg/lb) and Innovar-Vet* (1cc/20 lbs), intubated, and anesthetized with Halothane USP using the method described by McCahan.[5] All the hair was closely clipped with a #40 clipper head.[6] The total body surface area (TBSA) was determined using the method of geometric design.[7] In 30 animals a 40 to 50% of TBSA conflagration burn was inflicted with propane torches depending upon the configuration of the animal.

The Minipig was placed in a modified metabolic cage in our intensive care area and monitored for 48 hours. Data were obtained as indicated in Figure 2. Each animal was randomly assigned to one of six therapy groups and resuscitation was administered as follows:

GROUP I. Untreated, Non-Burned Controls: These subjects underwent all the anesthetics, procedures, and data collections as Groups II, III, IV, V, and VI, with the exception that they were not burned. They were offered water ad lib not to exceed 800 cc per eight hour shift. Only minimal amounts of intravenous and intra-arterial heparinized Lactated Ringer's were used to maintain catheter patency.

GROUP II. Burned, Non-Resuscitated: These animals were handled exactly as the controls (Group I) but were given a significant burn similar to Groups III, IV, V, and VI.

GROUP III. Burned, Resuscitated with "Brooke Formula": These swine were burned and then treated with Lactated Ringer's** and plasma in the volume indicated by the Brooke Formula modified to exclude the free water: i.e.,

1.5 cc Lactated Ringer's/Kg/1% burn
0.5 cc Plasma/Kg/1% burn

per 24 hours and one-half this regimen in the second 24 hours.

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*McNeil Laboratories, Ft. Washington, PA 19304

**Concentration of electrolytes (mEq/L): Sodium 130, Chloride 109, Lactate 28, Potassium 4, and Calcium 3.

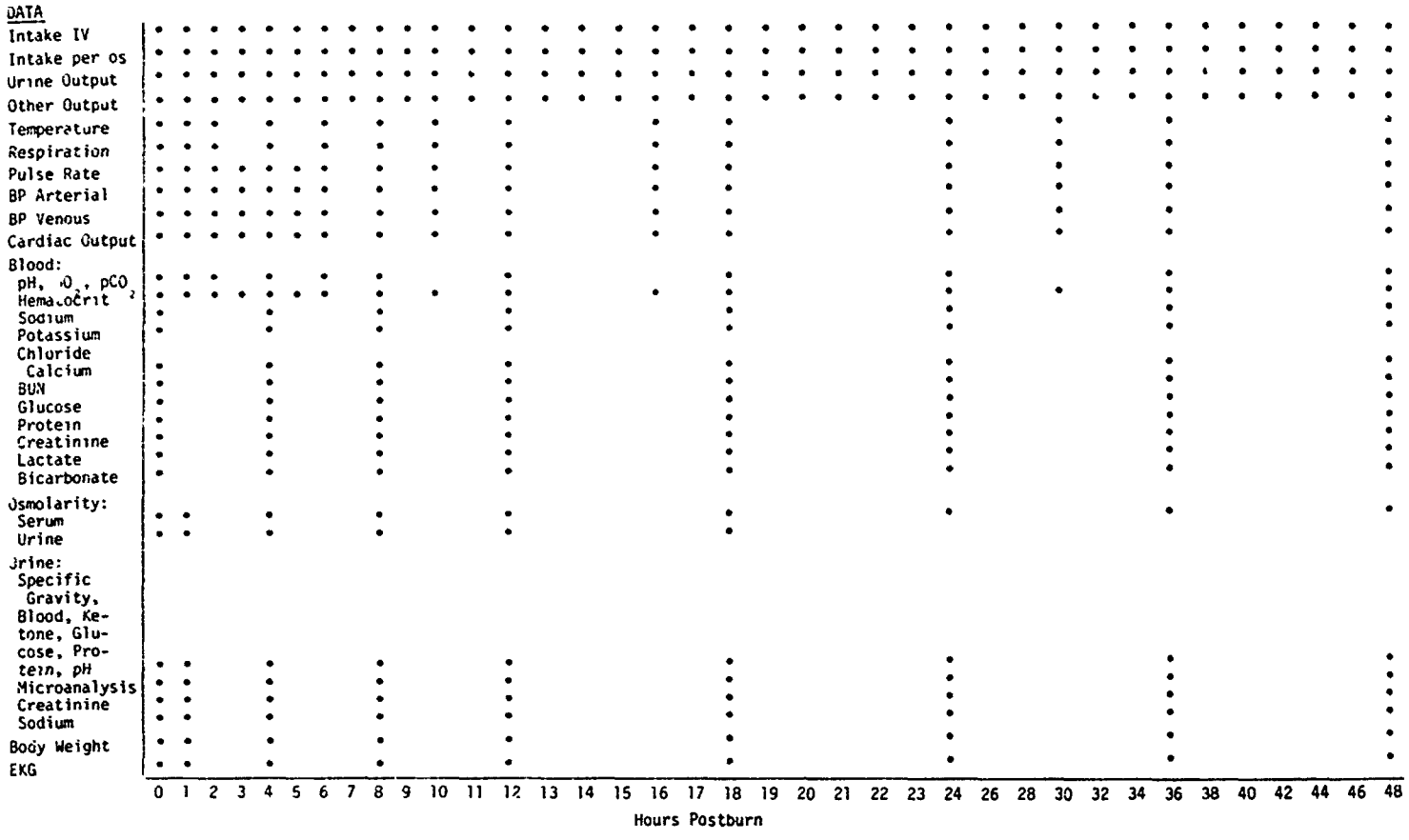

FIGURE 2. Data Acquisition by Chronological Reference

GROUP IV. Burned, Resuscitated with Lactated Ringer's: These burned miniature swine received the volume of Lactated Ringer's solution that would give the same amount of sodium intravenously as if they had received the "Brooke Formula." This amounted to nearly the same water and sodium loads as those in Group III, but did not use plasma.

GROUP V. Burned, Resuscitated with Hypertonic Lactated Saline (HLS): These animals received HLS containing:

Sodium	275 mEq/L
Lactate	125 mEq/L
Chloride	150 mEq/L

in amounts such that the sodium administered to them was the same as Group III.

GROUP VI. Burned, Resuscitated with Parkland Formula: This treatment group received 4 cc Lactated Ringer's per kilogram body weight per 1% burn.

A summary of the relative amounts of volume and sodium in each treatment group is shown in Table 1*. After the initial 48 hours the animal was returned to a 4x16 foot wire enclosed run with a sloped concrete floor. Each animal was checked periodically for activity, appetite, and general condition. All subjects had to survive an additional 48 hours, or a total of 96 hours post-burn, to be counted as a survivor. Each animal was necropsied at the time of death or at 96 hours to complement clinical and research data.

RESULTS

The group distribution, percent TBSA burned, initial body weights, volume and sodium load, urinary output, survival, and other data for individual animals are shown in Table 2.

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*All tables are listed in Appendix B.

The average percent of TBSA burned and percent survival for each therapy group are summarized in Table 3.

The average percent change in body weight for each treatment group is illustrated in Table 4.

Sodium and water balance values are given in Table 5. Table 6 illustrates the calculated insensible water loss. There is no significant difference among Groups II, III, IV, V, and VI.

Table 7 lists the range of normal values for each parameter monitored as derived from our baseline data acquisition and values reported in the literature.

Tables 8 and 9 show the mean vital signs for each treatment group versus time (the 48 hours of intensive care). The temperature dropped post anesthesia but thereafter was stable and within normal limits. The pulse rate was within the range of normal values throughout but was elevated from baseline data at four through 18 hours (Group II); four, six, eight, and 18 through 48 hours (Group III); and eight hours (Group VI). Respirations were always within normal limits. The blood pressures varied, but were in the normal range throughout and did not show any trend data for any groups or times. The pulse pressure was generally 45-50 mm Hg.

Cardiac output was determined by the dye dilution method using both the forward triangle[11] and Steward-Hamilton methods for determining the area under the curve. Figure 3 plots the cardiac output in percent of the preburn (and anesthesia) value versus time. These cardiac output determinations fell initially in all groups except Group VI. The control group remained between 90% and 100% of the pre-anesthesia value until after 16 hours, where it decreased to between 80% and 90%. Group II, who received no replacement therapy, decreased down to the 60% of preburn value and never recovered. Groups III and IV were similar initially; however, Group IV overshot 100% at about six hours postburn while Group III overshot 100% at about 16 hours and remained elevated during the second 24 hour period. Group V was the slowest of the treatment groups to return to 100% (30 hours) but was not significantly different from Groups III and IV at 48 hours. Group VI cardiac outputs were much greater than 100% from the onset of therapy through the initial 24 hours of treatment. During the second 24 hours the cardiac output decreased some, but remained significantly elevated above the preburn value.

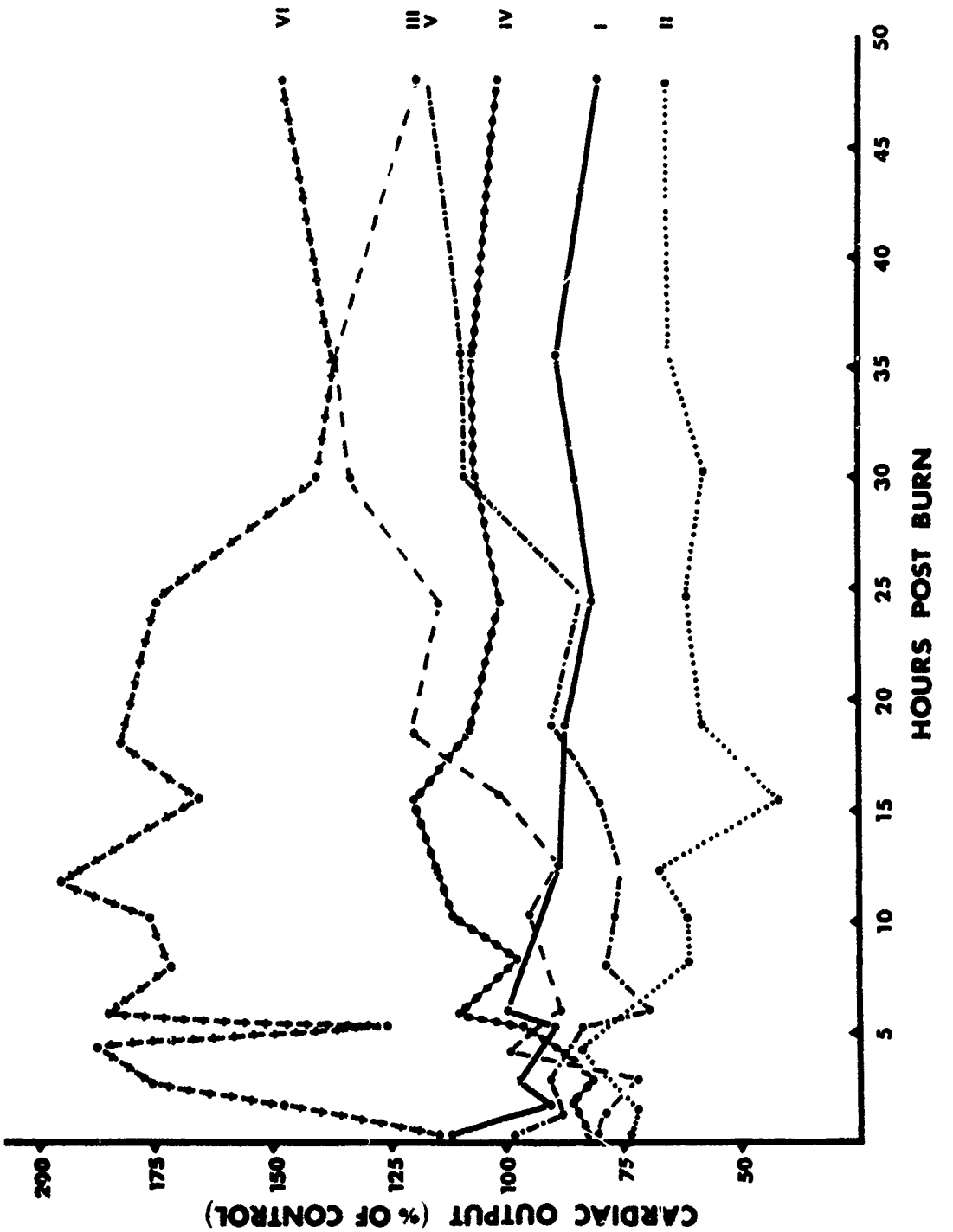

FIGURE 3. Cardiac Output for Each Group in Percent of Preburn (and Anesthesia) Value Versus Time

Serial hematocrit levels are given in Table 10. All groups showed significant anemia by 48 hours. There were no significant differences between groups.

Serum sodium values (Figure 4) show no significant differences between groups for the first 12 hours postburn. Thereafter, the HLS treatment group had elevated serum sodiums. Group III had slightly elevated serum sodiums the second 24 hours.

Urinary excretion of sodium is constant in the Controls (Group I), decreased in the Burn, Non-Resuscitated animals (Group II), and increased in those groups treated with saline solutions (Groups III, IV, V, and VI), especially during the second 24 hour period (Figure 5).

The percent of administered sodium load excreted in the urine for each treatment group is shown in Table 11. There was no significant difference among Groups III, IV, and V who received the same sodium dose. Group VI showed a slightly higher percentage.

Serum chloride is elevated in Groups III and V after 18 hours postburn (Table 12). Serum potassium (Table 13), calcium (Table 14), and bicarbonate (Table 15) remain within normal limits for all treatment groups during the entire intensive care period. Lactate values (Table 16) are normal even during large lactate loads. Glucose levels (Table 17) are within normal limits except for four diabetic pigs which are included in this study. The protein values (Table 18) are normal except for the middle portion of the intensive care period for Group VI. The BUN is normal (Table 19), except for the Burned, Non-Resuscitated (Group II) which showed a slight elevation during the second 24 hour period mainly due to higher levels in two very sick animals, one of which subsequently died. The serum creatinine (Table 20) is not elevated in any group. Urinary creatinine is shown in Table 21.

Serum and urinary osmolarity are given in Tables 22 and 23. Serum osmolarity was generally preserved within the normal range for all groups while urinary osmolarities varied and occasionally exceeded the normal range.

The arterial blood gas determinations are given in Table 24. All treatment groups were alkalotic. Groups I, IV, V, and VI were initially in metabolic alkalosis while Groups II and III were in respiratory alkalosis. Metabolic alkalosis and combined alkalosis predominated throughout the

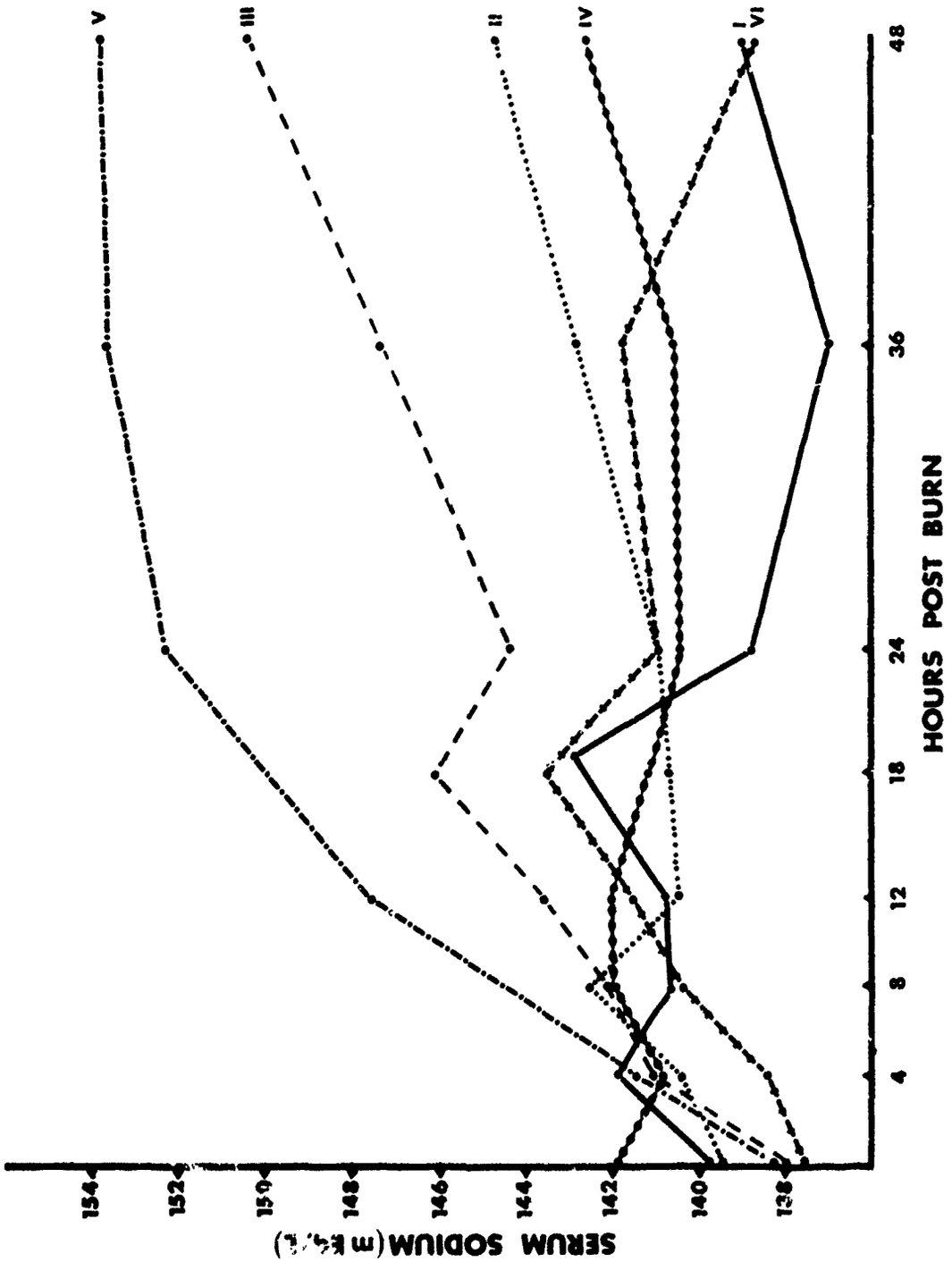

FIGURE 4. Serum Sodium Values

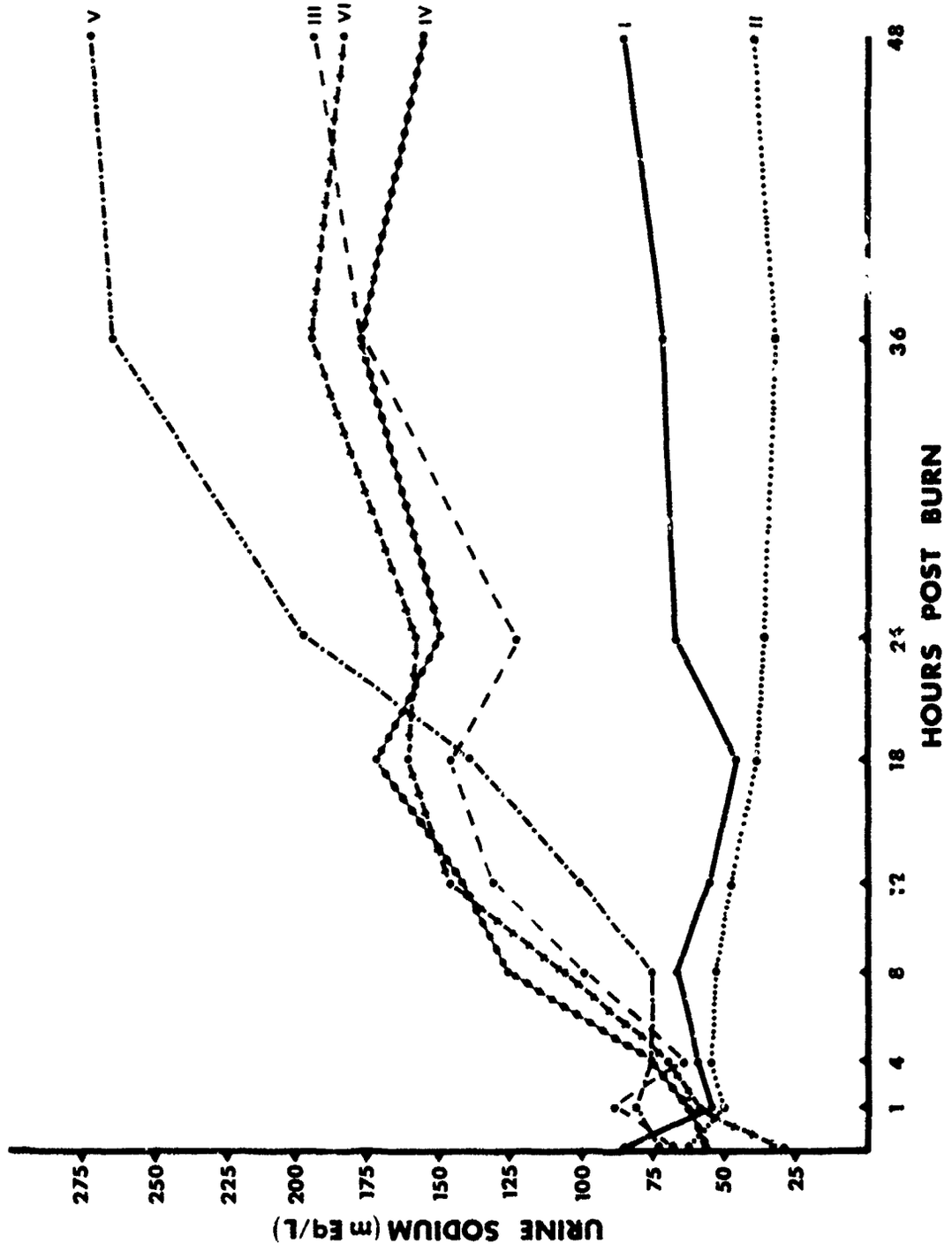

FIGURE 5. Urinary Excretion of Sodium

intensive care period.

The urinary specific gravity is given in Table 25. All burned animal groups concentrated their urine in the immediate postburn period and remained concentrated with the exception of Group VI which returned to preburn levels. The baseline urinary pH was six and remained acid in the Controls (Group I) and Burned, Non-Resuscitated subjects (Group II). It was neutral in Group VI and neutral or alkalotic in Groups III, IV, and V.

All data are presented as average values for each treatment group for each time. The statistical analysis was by multivariance techniques.

DISCUSSION

Many burn and hemorrhagic shock studies have been performed on the dog,[12-14] rats,[15-22] mice,[23-25] and monkeys.[26,27] No porcine burn shock models are known. However, the pig has had extensive investigation as a model for the cutaneous burn lesions and comparative analysis to human skin in both the normal and thermally injured condition. The fluid shifts within the burned and adjacent tissues more closely approximate that of the human. Their size and total blood volume are adequate. There is good theoretical evidence that the pig would be a more ideal model for burn shock research because its erythrocytes contain potassium (similar to human) which would release potassium and not sodium during hemolysis. They are reasonably economical and can be purchased in a miniature laboratory size for ease in care and handling. In addition, interest in this species has mushroomed recently and many normal and pathological physiological parameters have been investigated.

Moritz and Henriques[28] have described porcine skin before and after thermal exposures and compared it to human burns showing the relative vulnerability of porcine and human skin to thermal injury. They were able to show little or no quantitative differences in the susceptibility of human and porcine epidermis to thermal injury at similar surface temperatures. Moritz[29] delineated the pathogenesis and pathological characteristics of cutaneous burns in relation to the duration and intensity of thermal exposure and to their susceptibility for organization, repair, and healing.

Perkins, Pearse, and Kingsley[30] demonstrated comparative surface appearance and similar threshold and average values (cal/cm^2) for human

and porcine skin subjected to radiant energy, in epidermal and intradermal (and perhaps subdermal) burn lesions. Their data were comparable to the values of 2 cal/cm^2 for epidermal burns and 3.5 cal/cm^2 for deep intradermal burns in humans reported by Butterfield and Dixey.[31] They also correlated well with the 3.9 cal/cm^2/sec (0.54 sec exposure) figure for definite intradermal and 4.8 cal/cm^2 (0.54 sec exposure) value for subdermal human burns reported by Moncrief.[32]

The heat capacity and thermal conductivities of cutaneous and subcutaneous tissues of the pig, in vivo observations of caloric uptake of pigskin, rise in temperature at the dermis-fat interface as a function of both time and skin surface temperature and an estimation of the temperature changes at the epidermal-dermal interface during the exposure of the skin surface to heat have been reported.[33] Moritz, et. al.,[34] have investigated the mechanisms by which thermal exposures, in which heat is transferred to the body through an envelope of air, cause disability and death.

Comparative studies of the skin of the domestic pig and human have been reported by Montagna and Yun.[35] They noted that the skin of the pig shares anatomical and histochemical features with that of man although some other dissimilarities exist.

Kerr[36] presented the averages of determinations of potassium and sodium in erythrocytes in about 20 species of vertebrates. The pig (sus scrofa, melitensis) showed 99.5 mM potassium and 10.8 sodium per 1000 grams corpuscles; dog (canis familiaris), 8.7 mM potassium and 107.0 mM sodium per 1000 grams corpuscles; man, 109 mM potassium per 1000 grams corpuscles; and monkey (Macacus), 111.5 mM potassium per 1000 grams corpuscles. Using flame photometry, Overman and Davis[37] found 437 (425-444) mg/100 ml potassium and 14 (trace to 31) mg/100 ml sodium in human RBC's and demonstrated that the potassium and sodium concentrations of the baboon, rabbit, rat, and horse RBC's were similar to that of human erythrocytes. The pig apparently was not investigated in their study.

On the weight of the aforementioned evidence we believed that the pig and in particular the miniature swine should be investigated and developed as a large animal (comparable to man in size) burn shock model and initiated this pilot study.

Selecting the mode of thermal injury is important since Fox[26] in a standardized full thickness scald and flash burn model in monkeys (Macacus

mulalta, irus) found that each type of burn required a different fluid regimen but was unable to delineate the true nature of the pathological physiology of deep burns of an effective therapy for flame burns. Commercially available propane torches have a high flame temperature and produce a full thickness burn in a relatively brief time simulating the flash flame burn often seen in human patients with thermal injury to the integument. With relatively little training one could produce a uniform burn over a previously determined area of the swine. Attempts in using infra red torches were successful in producing a full thickness burn but were somewhat slower, required special eye protection for both the researchers and animal, and caused thermal changes in the subcutaneous fat by the time the desired thermal injury to the skin was reached. Scalds were not attempted since we did not wish to study scald burns in this model at the present time.

The time for evaluation and monitoring was based on the usual period of intense hemodynamic change in burned patients of 48 hours. While this is by no means the end of such changes it is longer than most experimental evaluations. Additional time of less intensive observations was added because an impressive clinical report revealed that 74% of all burn fatalities occurred within the first three days.[38] Lyon, et. al.,[39] also showed that 40% to 50% body surface area burns in swine caused a significant mortality within 96 hours. The selection of parameters to monitor was determined mainly on those parameters that are evaluated clinically in burned patients and experimentally in other animal models.

To expand and develop this model it was necessary to use fluid regimens now in use in other animal models and clinical settings. Those fluid therapies chosen were selected to represent popular usage but divergent points of view. However, we are always admonished to use any formula only as a "rule of thumb" and to modify it as clinical judgement would indicate from all the evidence available. Nevertheless, for the study of the basic effects of a given fluid regimen a set protocol is desirable. This is especially true when the burn shock animal model is new and the pathophysiology and hemodynamics are sketchy. For this reason our initial experiment was determined by these "formulae" which set basic guidelines for the treatment of most severely burned human patients.

There is abundant evidence that the shock that regularly attends severe burns can be successfully treated with a variety of intravenous fluids.[17,32,40-56] Controversy still exists over the best fluid replacement scheme, type of fluid (electrolyte, colloid, or blood) and quantity to be

administered.[15, 23, 32, 40-44, 57, 58] Despite the improvements in the treatment of burn shock there are those who believe that the addition of colloid (plasma, albumin, dextran, blood)[5, 40, 44, 54, 55, 59] to solutions of sodium salts is necessary or desirable for the satisfactory initial resuscitation of patients with extensive burns, and those who favor only the use of crystalloids (lactated Ringer's injection, USP,[46, 58] and/or saline solution[13, 41, 43, 47, 48, 50, 56]). Because of the many unsolved biological problems the treatment of burn shock is largely empiric and not truly physiological. What is termed "resuscitative" fluid therapy is actually often precautionary or prophylactic since almost all modern fluid therapy, properly used, will prevent the appearance of clinical shock. Nevertheless, misconceptions and mismanagement still exist.

Although no comparative studies have been published, some investigators object to the possible risk of cardiovascular overload with interstitial pulmonary edema and local deleterious effects on the wound resulting from the necessarily larger net fluid loads when crystalloid alone is used.[40] The "crystalloid" proponents believe that in addition to clearly demonstrated physiological benefits of the crystalloid solutions in acute thermal injury, simplicity, elimination of the risk of serum hepatitis,[60, 61] and decreased cost are important factors.

The fall in plasma volume, once thought to be the genesis of the clinical syndrome of burn shock, is probably not a vital determinant[66] since concurrent objective clinical improvement in the face of falling plasma volume is regularly observed. Moncrief, Pruitt, and Mason[51] demonstrated that fluids administered within the first 24 hours principally increased the amount of edema and augmented the blood volume little or not at all. They indicated an obligatory, relentless volume loss during the first 24 hours that was independent of the composition of the fluid being infused. They showed that leakage rates were less than infusional rates during the second 24 hours, suggesting that a redistribution of corporeal fluid was then occurring.

Rhoads, et. al.,[67] found that plasma administered to burn patients did not yield the predicted rise in plasma volume until 36 to 48 hours postburn when spontaneous augmentation of blood volume begins to occur no matter what crystalloid or colloid has been given.

Two major controlled alternate case studies of the therapy of burn shock were conducted in Peru by Markley and associates. In the first study[52]

either balanced saline solution (equal to 15% body weight) per os or intravenously or plasma with additional glucose and water (equal to up to 10% body weight) was given during the first 48 hours. None of the 79 patients treated with balanced saline solution died while 12% of the 74 patients treated with plasma and glucose died. In the second study[53] a modified Evans' formula (1 ml plasma/Kg body weight/1% body surface burn and enough additional balanced saline solution up to the amount of 15% of the body weight to maintain an adequate urine flow) was substituted for the plasma and glucose. There was no statistically significant difference in mortality between the two groups in the second experiment, except in children under age four years with greater than 30% BSA burn. Some studies have shown plasma therapy to be disadvantageous in the treatment of thermal burns.[56,68]

Fox observed that patients with extensive burns treated with saline solutions alone did as well as patients treated with saline plus colloids.[49] We were unable to detect any significant differences between the group receiving plasma and the groups receiving saline solutions alone.

The use of solutions containing sodium salts in the treatment of burn shock has become firmly established in clinical practice.[1] Sneve first reported that orally and rectally administered normal saline solutions prevented death from burn shock and suggested saline transfusions in 1905.[45] Other investigators have confirmed these observations and observed that intravenous saline solutions are of definite value in the treatment of burn shock.[23-25,41,43,46-50,62,63]

Large positive sodium loads (1000-4000 mEq for adults) are necessary during the first 48 hours for successful resuscitation although there are somewhat unpredictable variations for each individual.[1,64] Most of the sodium load is necessary during the first 24 hours although subsequent sodium therapy is required to maintain the sodium balance even though hyponatremia may persist. Darrow and Yannet showed that the removal of sodium promptly leads to shock and circulatory collapse.[65]

Thus, sodium is the one important factor in the treatment of burn shock and all resuscitation techniques include some concentration of sodium within the volume replacement. Our unburned and burned Controls (Groups I & II) received very little sodium during the experiment, but all other treatment groups were given a large sodium load consistent with usual clinical methods. The net sodium balance was positive in all groups

(Table 5) during the initial 24 hours and for the entire 48 hour period of intensive care and monitoring in all but Group I. There was some significant difference between Group III and Groups IV, V, and VI during the first 24 hours with the latter being 39% to 109% greater; however, there were no significant differences when the entire 48 hour period of intensive care and monitoring was considered.

Why burned tissues display an avidity for water, minerals, and albumin in different proportions from those in blood plasma or interstitial fluid is still unknown. Plasma albumin accumulates promptly in the area of the burn but initial serum protein concentrations are usually normal, suggesting parallel movement of water and protein into the wound. The thermal injury to the epithelium of the vascular walls demonstrated by electron microscopy provides a possible explanation for the "molecular sieving" effect.[1] These thermally injured capillaries probably leak endogenous and exogenous albumin by the same mechanism during the initial 24 hours postburn.[1] If one assumes that the Starling Hypothesis holds, this increased amount of sequestered extracellular albumin would cause an increased tissue colloid osmotic pressure which would result in the flux of water into the wound. On the other hand Fox[50] believes that the acquisition of sodium by injured cells reduces the tonicity of the extracellular fluid and this, together with the increasing hydrogen ion concentration (H+) of cells, causes uninjured cells to imbibe water. The intracellular gain in water from hypotonic extracellular fluid was demonstrated by McCance[69] to result in decrease in plasma volume without prior plasma loss.

This does not explain the entire mechanism for the efficacy of sodium containing fluids although several investigators maintain that corporeal sodium mass is an important determinant of plasmatic volume and that sodium is requisite for normal cellular metabolism.[41,46,47,62,65,70]

Fox[50,62,63] and Moyer[46] have shown that proportionately more sodium than water is sequestered during the marked fluid shift into traumatized tissues but the precise anatomical location of the traumatic edema fluid and of its solutes has not been elucidated.

Hypotonic sodium salt solutions (i.e., lactated Ringer's) produce unnecessarily voluminous wound edema because they contain more water and less sodium than does the fluid sequestered into the wound.[1,71] Thus, to provide an adequate sodium load, more water than is minimally necessary must be given which may be deleterious to extensively burned patients or

those with pre-existing cardiovascular disease. "Free" water magnifies this error.

A certain volume of water (approximately 10% to 15% of the body weight during the first 24 hours and 5% or less during the second 24 hours) is necessary,[1,50] but the administration of "free" water to account both for normal insensible water loss and for increased transcutaneous water vapor is unsubstantiated.[1]

Hypertonic saline solutions[17,22,23,41,44,47] would seem to provide a more favorable Na/H_2O ratio which would be in concert with the fact that more sodium than water is sequestered. The use of hypertonic saline solutions has been reported in experimental and clinical hemorrhagic and burn shock, but they have not yet received adequate trial in burns and warrant further intensive study to determine the optimal ratio. Unfortunately, little is known about the overall consequences of one or the other modes of early treatment.

The hyponatremia of acute burns tends to affirm the desparate egress of sodium and water from the plasma. Perhaps starting treatment solutions immediately postburn masked that hyponatermia since the serum sodiums in our model were not depressed and, in fact, reflected the concentration of the infusing solution to some extent rather than the positive sodium loads. The HLS (Group IV) showed significantly higher values during the second 24 hour period of monitoring. This is not easily explained since the number of milliequivalents of sodium/Kg/1% body burn were kept equal in Groups III, IV, and V. Group III shows some elevation at 48 hours; however, the other four treatment groups showed no significant differences.

The urine contains practically no sodium in humans following severe burns. In our experiment there was extreme conservation of sodium in the unburned and burned controls which received very little sodium (most of their fluid intake was sodium free tap water per os). The urinary sodium reflected the positive sodium load in the four treatment groups by higher urinary sodium values. The HLS (treatment Group V) was the highest of these, especially during the second 24 hours.

The sodium balance is further defined by the percent of the infused sodium load excreted in the urine. All groups conserved sodium during the initial 24 hours. Thereafter, the Controls (Group I) excreted far more sodium than they were given albeit the amount is still relatively small

despite the percentages (343% and 142%). The Burned, Non-Resuscitated Group (II) also excreted more than the input during the second 24 hours as indicated by both the percent of sodium load excreted (Table 11) and by the sodium balance (Table 5). There is remarkably little difference in the percent of sodium load excreted for the entire 48 hour ICP for Groups III, IV, and V which is consistent with the sodium loading. Group V showed an initial conservation of sodium which is reflected by the higher sodium retention (Table 5) and the low percentage of sodium load excreted (24%); however, an excess of the excess sodium was present in the second 24 hours of the ICP. Group VI with the highest sodium load showed a slightly higher excretion percentage.

It has been shown that burned human and animal skin becomes almost immediately porous to water vapor, probably due to loss of lipid from the epidermal layer.[1] Our calculated "insensible water loss" showed an expected increase in all the burned animals compared to the Control Group. The ratio of this difference was two or three to one during the second 24 hours. These observations provide at least a partial explanation for the dramatic weight loss shown in all animals (except for Group VI) in spite of a positive water balance. To our knowledge accurate measurements of the rate of insensible transcutaneous water vapor loss through the burned skin have never been made in acutely burned swine.

Even considering the increased rate of insensible transcutaneous water vapor loss through the burned skin, the majority of the fluid is sequestered locally and not lost into the environment. The drastic internal translocation of water, minerals, and protein that is known to occur after cutaneous thermal injury helps to explain our positive water balance over and above that shown by the Controls.

Moylan, et. al.,[2] have evaluated the individual contributions of sodium and volume to resuscitative effect as measured by the restoration of cardiac output in scalded dogs. They estimate that one milliequivalent per kilogram sodium exerts an effect on cardiac output equalled by 13 ml/Kg of volume. Using these estimates the following data can be derived from our figures and the equation

$$R = \frac{\text{ml fluid/Kg/day}}{13\ \text{ml}} + \text{ml fluid/Kg/day} \times \text{mEq Na+/ml}$$

where R equals the relative value of restoration of cardiac output.

Group III animals received a fluid volume of 92 ml (2 ml/Kg/average body burn of 46%). Because the sodium levels of the infusion plasma were nearly equal to lactated Ringer's, Group IV subjects also received 2 ml/Kg/1% body burn or 88 ml (based on an average burn of 44%). To maintain a sodium load similar to Groups III and IV, Group V pigs required only a milliliter of volume or 40 ml/Kg (based on an average burn of 40%) which is approximately one-half the fluid load of Groups III and IV. In Group VI the volume was set by protocol at 4 ml lactated Ringer's/Kg/1% body burn or exactly twice the volume of Groups III and IV and four times that of Group V. Thus, these animals received a 184 ml/Kg fluid load (based on an average burn of 46%) and the sodium load was twice that of Groups III, IV, and V.

Hence for:

$$\text{Group III:} \quad R = \frac{92}{13} + (92 \times .13) = 19.04$$

$$\text{Group IV:} \quad R = \frac{88}{13} + (88 \times .13) = 18.21$$

$$\text{Group V:} \quad R = \frac{40}{13} + (40 \times .275) = 14.08$$

$$\text{Group VI:} \quad R = \frac{184}{13} + (184 \times .13) = 38.07$$

Therefore, Group VI should have the highest cardiac output because of the high volume and sodium load; Group II, the lowest; and Groups III and IV, approximately the same, with Group V also in the range of III and IV. This was indeed the case. Burned, Non-Resuscitated animals were unable to restore the cardiac output and all other groups were able to restore and overshoot the expected 100% original cardiac output. The HLS Group (V) was the slowest and Group VI the most rapid.

Evaluation of some of the other parameters amplifies and confirms some of the well known responses to the various treatment regimens in clinical and experimental applications and serves to compare the response in the miniature swine burn shock model to them.

In otherwise stable patients urinary output has been a good practical indicator for altering the rate of fluid administration,[1] although it errs on

the side of over-hydration.[2] The urine output was lowest in the Burned, Non-Resuscitated animals (Group II) but did not approach oliguria, perhaps as a result of the oral fluid intake. Scanty urinary output is generally attributed to fluid shifts with a decreased blood flow to the kidneys and decreased glomerulofiltration rate and increases in the blood concentrations of catecholamines, aldosterone and antidiuretic hormone in acute, severe burns.[1] The HLS treatment group (Group V) had slightly more urinary flow than the Controls (Group I) but only about two-thirds that of Groups III and IV. Group VI had a significant polyuria which was five times the Control and represented a function of over-hydration.

Indirect measurement of blood pressure is not always obtainable in a severely burned patient whose limbs are involved and routine cannulation for these readings is avoided for fear of invasive infection.[1] When the blood pressure is measured it is usually normal or low, depending upon the time that has elapsed since the injury (burn) and the adequacy of the treatment administered. Our animals showed no trend data although Group VI was over-hydrated and Group II, perhaps, grossly under-hydrated.

The pulse rate may be rapid when treatment has been delayed but should be stable and approach a normal rate as treatment progresses unless complications occur or treatment is uneffective. Pulse rates were elevated in several groups, perhaps indicating the planned ineffective treatment of Group II and excitement and/or technical errors in other groups.

The design of the modified metabolic cage was primarily predicated on the effect that other restraining methods (i.e., slings, harness, etc.) would have on the respiratory system. The cage allowed movement fore and aft and up and down but did not allow the animal to turn around and foul the instrumentation. A properly equipped totally free roaming animal would be the ideal preparation.

Thermal respiratory injury was avoided by the torch method of inflicting the burn. Also, care was taken not to create constrictive circumferential eschars about the torso by allowing the entire ventral surface, axillae and groins to remain unburned.

The tachypnea which is often present in anxious, previously untreated patients[1] did not appear often in our subjects (Table 8) even in Group II. There were relatively rapid but transient increases in respiratory rate, blood pressure, and heart rate in individual animals who were excited.

The circulating red cell mass is normal or slightly decreased presumably due to thermal destruction of red blood cells trapped in the area of the burn. However, this erythrocytolysis is not ordinarily of sufficient magnitude to offset the loss of plasma water that also occurs, so the hematocrit is normal or high and the rise occurs soon after burn injury, but may not be a reliable reflection of the plasma volume during burn shock.[1] All of our treatment groups had stable postburn values except the Burned, Non-Resuscitated Group (II) which had a slight but not significant rise. Perhaps the oral intake added volume to the circulation as observed by Sneve.[45] The anemia which developed may have been iatrogenic in that nearly 300 cc of blood were removed from each animal for laboratory studies. This is borne out by a significant but less severe anemia developed in the Controls (Group I). Red cell destruction may account for the additional 7 to 10% decrease in hematocrit in the burned animals. Future studies would utilize animals with greater initial hematocrit values and prescribe less vigorous phebotomy methods for laboratory evaluations

Hemoglobinuria may result from erythrocyte dissolution and appear as red urine early in the course of a severe burn or in untreated patients.[1] Our studies reflected this finding.

Serum chloride elevations to slightly above the normal range might be expected in Group V because of the larger chloride load in the infusing solution but were surprising in Group III. Despite the elevation above the normal range it was not significantly different from the values of the other groups (excluding Group V). Fox[72] has placed emphasis on higher chloride levels in the infusing solution to provide a more optimal hypertonic lactated saline solution for burn shock resuscitation. He recommends 150 mEq/L.

Normal potassium concentrations were observed throughout the entire study. The hyperkalemia due to release of intracellular potassium from injured cells, including erythrocytes (K^+ laden in swine) probably was avoided by normal kidney function. Thus, cardiac arrhythmias due to hyperkalemia were not present.

Hypocalcemia generally occurs only in patients with extensive thermal injury to the subcutaneous fat (suponification). There was no significant change in the serum calcium levels for any treatment group although Groups II and V did show a slight decrease. This difference might be explained by the fact that intravenous administrations of small amounts of calcium salt were given in Groups III, IV, and VI (via lactated Ringer's) and Group I did not receive any thermal injury.

Mild azotemia was found only in the Burned, Non-Resuscitated Group (II). Such changes may occur as a result of cytolysis at the site of the injury and can be considered an artifact in part related to plasmatic dehydration.[1]

The baseline alkalotic status of these miniature swine may have offset the metabolic acidosis which regularly develops within a few hours after burning due to the accumulation of fixed acids released from injured tissues and to ineffective tissue perfusion.[1] The lacticemia which may result from impaired perfusion of muscle or viscera did not attend any group in this study. The plasma CO_2 content which is often low in severe burns was normal in all of our treatment groups.

The stainless steel implanted limb electrodes provided a convenient and reliable method for applying the ECG instrumentation. Chronic implantation caused no irritation and served as a pilot study for long term implantation of platinum-irridium electrodes in human subjects.[73]

A gallop rhythm or other arrhythmia should always be considered abnormal since neither occurs in the ordinary case.[1] Tachycardia was the most frequent arrhythmia in our study. Premature ventricular contractions occurred occasionally but could not be correlated with the burn injury or treatment regimen. The ECG monitoring was helpful in determining ventricular fibrillation as the cause of death in one animal.

The mortality figures have very little overall significance because of the small number of animals in each group. However, it is relatively significant that one-half the animals in the Burn, Non-Resuscitated (Group II) treatment group died, especially in light of the fact that two of the three survivors were obviously very ill and undoubtedly would have died had the empirical termination time for the experiment been greater than 96 hours postburn. All other groups could well have had 100% survivability from burn shock as is expected from any of these therapeutic regimens used clinically for persons sustaining major thermal injuries to the skin and no other complicating factors. The two deaths from HLS each died acutely; one from ventricular fibrillation and the other following a grand mal convulsion. We believe that these may have been technical errors, probably from acute left heart or arch aortic infusion of the hypertonic treatment solution. The deaths in the "Brooke Formula" (Group III) treatment group all occurred after the animal had deteriorated for a longer period of time, but since all the deaths were early in the experiment when we were experiencing difficulty in obtaining and preparing porcine plasma, this

possible explanation is suggested. Our data suggest that all the clinical therapy regimens used in this experiment can be effective although greater numbers of animals would have to be used to show supremacy of one regimen over the others and complicating factors (such as heart failure, kidney impairment, etc.) would need to be considered.

We believe our data provide strong evidence in favor of using a miniature swine burn shock animal model. They show that miniature swine are sensitive to the burn injury and do go into burn shock which is fatal if the animal is not resuscitated with intravenous fluids. We recommend that additional, more extensive evaluations of controversial fluid regimens be submitted to experimentation using this animal model and that automated treatment techniques[74-78] be applied to this model to delineate the subtle burn shock problems, resulting in better overall treatment regimens in burn patients.

CONCLUSIONS

Swine, and in particular miniature swine, are a sensitive and responsive animal for the study of burn shock resuscitation and merit further experimentation.

The sodium loads requisite for resuscitation of burned swine can exert roughly the same effects when administered in volumes of from 25% to 50% less than those commonly employed clinically.

Sodium excretion is more dependent upon the sodium load than upon the concentration of the saline solution.

Plasma administration had no demonstrable resuscitative effect over and above that provided by the sodium and volume given in this model.

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APPENDIX A

EQUIPMENT LIST

Equipment	Manufacturer and Address
Tycos Hg BP	Taylor Instrument Companies Rochester, NY 14601
TR888	Gulton Techni-Rite Electronics, Inc. Warwick, RI 02887
Gilford Constant Flow System 105-S Gilford Cuvette Densitometer, Model 103-1R	Gilford Instrument Laboratories Oberlin, OH 44074
Veterinary Precision Surgical Thermometer	Industrial Scientific Research Corporation Anaheim, CA 92803
Physiological Monitor, Type 410	Tektronix, Inc. S. W. Millikan Way P. O. Box 500 Beaverton, OR 97005
Numechron Tymeter	Tymeter Electronics Pennwood Numechron Company Pittsburgh, PA 15221
Honeywell Visicorder Oscillograph, 115V 8 Amp 60 Cycles, Model 906C-179XF0J Honeywell Galvonometer Control, 117V 15 Amp 60 Cycles	Honeywell, Inc. Denver, CO 80201
Plastic Disposable 3-Way Stopcocks	Travenol Laboratories, Inc. Morton Grove, IL 60053
Statham Physiological Pressure Transducer, Model P23BB (Venous) and P23Db (Arterial)	Statham Laboratories, Inc. Hato Rey, Puerto Rico

APPENDIX B

TABLES 1-25

	Treatment Group	Relative Amounts of Constituents In Therapy Solution	
		Volume	Sodium
I.	Control	0	0
II.	Burn, Non-Resuscitated	0	0
III.	"Brooke Formula"	2	1
IV.	Lactated Ringer's	~2	1
V.	HLS	~1	1
VI.	Parkland Formula	4	2

TABLE 1. Summary of Relative Volume Ratios and Sodium Ratios Among Treatment Groups

Treatment Group	Pig No.	Sex	Age (Mo)	TBSA (M²)	% Burn	Initial Body Wt (Kg)	First 24 Hours Intake Volume	First 24 Hours Intake Na+	First 24 Hours Urine	Second 24 Hours Intake Volume	Second 24 Hours Intake Na+	Second 24 Hours Urine	Total 48 Hours Intake Volume	Total 48 Hours Intake Na+	Total 48 Hours Urine	Survival
I. Control	156	F	22	1.21	0	61.0	2588	60	1026	925	36	1235	3503	96	2261	Yes
	157	F	20	1.14	0	50.7	994	64	927	1475	16	915	2469	80	1842	Yes
	170	M	6	.73	0	23.7	499	52	144	635	18	793	1134	70	937	Yes
II. Burn, non-Resuscitated	142	F	24	1.24	42	66.1	958	60	945	120	16	704	1078	76	1649	Very Ill
	133	F	23	1.36	45	83.7	576	75	1260	0	0	60	576	75	1320	24 Hours
	147	M	21	1.09	31	47.7	2450	55	1423	1321	22	1308	3771	77	2731	95 Hours
	150	M	21	1.19	27	50.0	2477	65	990	1191	18	1127	3668	84	2117	Yes
	176	F	5	.74	45	22.5	1887	61	488	----	----	----	----	----	----	17 Hours
	167	F	20	1.14	45	48.1	1172	42	647	605	14	810	1777	56	1457	Very Ill
III. 'Brooke Formula'	135	M	25	1.26	47	64.4	6005	793	3148	----	----	----	----	----	----	24 Hours
	148	M	22	1.31	50	61.6	6204	810	2278	----	----	----	----	----	----	24 Hours
	159	F	21	1.41	44	66.7	5851	773	2745	2964	392	1730	8815	1165	4475	Yes
	161	F	20	1.41	42	72.0	2672	352	323	----	----	----	----	----	----	9 Hours
	166	F	20	1.33	46	62.7	5639	745	2990	3050	402	1895	8689	1147	4885	Yes
	179	F	6	.73	40	22.4	1579	209	754	884	107	441	2463	316	1195	Yes
	180	F	5	.73	44	20.9	1771	234	880	1001	113	395	2772	347	1275	Yes
IV. Lactated Ringer's	131	M	22	1.33	47	63.0	7062	918	4230	3363	437	3315	10425	1355	7545	Yes
	138	F	24	1.34	44	62.3	8782	1142	2105	2833	386	2400	11615	1510	4505	Yes
	144	M	22	1.24	34	56.2	5771	750	2585	2775	361	3560	8546	1111	6145	Yes
	153	F	23	1.32	53	67.7	7571	984	2010	3603	468	1320	11174	1453	3330	Yes
	175	M	5	.74	47	24.9	2290	298	799	1300	169	450	3590	467	1249	Yes
	256	F	22	1.21	41	53.1	5010	651	2437	2430	316	2545	7440	967	4982	Yes
V. HLS	130	M	24	1.21	41	53.6	2345	704	1515	1402	421	1690	3747	1124	3205	Yes
	136	M	23	1.26	35	64.9	3480	921	1496	1656	450	2065	5136	1372	3561	Yes
	141	M	22	1.26	46	53.1	1089	260	580	----	----	----	----	----	----	10 Hours
	152	M	22	1.31	30	57.6	2645	727	1605	1385	381	2435	4030	1108	4030	Yes
	164	F	20	1.29	45	56.7	2210	575	1170	1439	374	890	3649	949	2060	Yes
	173	M	6	.72	46	25.5	1104	303	498	404	111	400	1508	414	898	40 Hours
	174	M	6	.77	40	25.0	869	239	536	525	144	600	1394	383	1136	Yes
VI. 'Parkland Formula'	143	F	22	1.22	48	50.5	9614	1250	5545	4995	649	4620	14609	1899	10165	Yes
	151	M	22	1.21	46	56.1	9963	1295	2977	5022	652	4365	14985	1948	7342	Yes
	160	F	20	1.28	47	59.4	10608	1379	6735	5580	725	4730	16158	2104	11465	Yes
	172	F	6	.75	41	23.5	3434	447	1055	2093	2772	1260	5527	719	2315	Yes

TABLE 2. Data Summary of Individual Animal Statistics with Volume and Sodium Load and Urinary Output

	Treatment Group	Number of Subjects	Average % of TBSA Burned	Survival %
I.	Control	3	0	100
II.	Burn, Non-Resuscitated	6	39	50
III.	"Brooke Formula"	7	46	59
IV.	Lactated Ringer's	6	44	100
V.	HLS	7	40	71
VI.	Parkland Formula	4	46	100

TABLE 3. Summary of Percent TBSA Burned and Survival for Each Treatment Group

	Treatment Group	Average % Δ Weight In 24 Hours	In 48 Hours
I.	Control	- 5.6	- 7.7
II.	Burn, Non-Resuscitated	-13.9	-13.2
III.	"Brooke Formula"	- 5.6	-11.2
IV.	Lactated Ringer's	- 0.6	-15.1
V.	HLS	- 7.0	-12.7
VI.	Parkland Formula	+ 0.8	- 2.8

TABLE 4. Average Percent Change in Body Weight for Each Treatment Group

Treatment Group		Volume (ml/Kg) First 24 Hrs	Second 24 Hrs	Total	Sodium (mEq/Kg) First 24 Hrs	Second 24 Hrs	Total
I.	Control	14	3	17	0.73	-1.02	-0.29
II.	Burn, Non-Resuscitated	19	-2	17	0.71	-0.14	0.57
III.	"Brooke Formula"	46	21	67	5.82	2.11	7.93
IV.	Lactated Ringer's	67	10	77	8.07	0.32	8.39
V.	HLS	19	-4	15	9.51	-0.34	9.17
VI.	Parkland Formula	93	17	110	10.82	-1.54	9.28

TABLE 5. Sodium and Water Balances: Average Values for Each Group for the Initial and Second 24 Hours and Total 48 Hours

Treatment Group		Insensible Water Loss First 24 Hours	Second 24 Hours	48 Hours
I.	Control	70	24	94
II.	Burn, Non-Resuscitated	158	-9	149
III.	"Brooke Formula"	102	77	179
IV.	Lactated Ringer's	73	55	128
V.	HLS	89	53	142
VI.	Parkland Formula	85	53	138

TABLE 6. Insensible Water Loss (ml/kg) Derived from the Change in Measured Body Weight (Table 4) and Water Balance Data (Table 5)

Constituent	n	Average (Range)	Units	Reported Values
Rectal Temperature	33	38.5 (35.5-40.5)	°C	38.3 ± 0.2*
Pulse Rate	33	125 (70-200)	bpm	124 ± 3**
Respiratory Rate	33	15 (6-35)	bpm	
BP (Arterial)	33	149/98 (110/50-195/150)	mm Hg	
(Venous)	33	-5/-14 (-10/-32 ↔ +6/+4)	mm Hg	
Cardiac Output	30	7.23 (3.72-11.51)	L/min	5.34 ± 0.2**
Cardiac Index	30	5.66 (2.22-8.14)	L/min	4.76**
Hematocrit	33	34 (30-39)	o/o	46 ± 0***
Sodium (Serum)	33	139 (135-145)	mEq/L	
(Urine)	27	51 (6-178)	mEq/L	
Chloride (Serum)	33	99 (89-106)	mEq/L	
Potassium (Serum)	33	4.4 (3.9-5.2)	mEq/L	
Calcium (Serum)	33	9.0 (7.2-10.8)	mEq/L	9.3 ± 2.3***
Bicarbonate (Serum)	30	23 (20-38)	mEq/L	
Lactate	20	19 (6-35)	mg/100 ml	
Glucose	29	104 (65-130)	mg/100 ml	43 ± 16***
Protein	33	7.5 (6.2-8.4)	g/100 ml	7.3 ± 0.8***
BUN	33	18 (11-26)	mg/100 ml	17 ± 2***
Creatinine (Serum)	33	1.3 (0.8-1.7)	mg/100 ml	1.1 ± 0.3***
(Urine)	24	99 (16-260)	mg/100 ml	
Osmolarity (Serum)	33	304 (266-331)	mOsm/L	
(Urine)	33	550 (124-994)	mOsm/L	
pH (Arterial)	32	7.56 (7.50-7.62)		
pO_2 (Arterial)	32	72 (52-94)	mm Hg	
pCO_2 (Arterial)	14	32 (15-45)	mm Hg	
Urine Specific Gravity	30	1.016 (1.004-1.030)		

TABLE 7. Normal Values for Miniature Swine (n) Vital Functions and Blood and Urine Constituents (*Reference 8; **Reference 9; ***Reference 10)

Treatment Group	Vital Sign	Time Postburn (Hours) 0	1	2	4	6	8	10	12	18	24	30	36	48
I. Control	T	40	37	39	39.5	40	39	40	39	39.5	38.5	39	39.5	39.5
	P	140	120	117	115	125	111	132	103	116	106	109	133	119
	R	15	16	27	20	36	14	12	11	15	12	10	12	12
II. Burn, Non-Resuscitated	T	38	36	36.5	38	38	37	37.5	38	38	37.5	37	38.5	37.5
	P	116	141	112	141	153	146	147	144	150	130	136	136	135
	R	12	9	12	13	11	15	9	15	14	12	9	10	13
III. "Brooke Formula"	T	38.5	38.5	39	39.5	40	39.5	39.5	39.5	39.5	39	40.5	39.5	39
	P	126	139	138	164	154	150	137	153	151	150	163	183	157
	R	21	19	21	19	17	16	14	14	17	17	13	15	14
IV. Lactated Ringer's	T	37.5	37	38	39	38.5	38.5	38	39	39	38.5	39	39.5	38.5
	P	107	104	120	136	138	113	107	120	110	120	120	129	136
	R	15	12	15	13	11	11	13	11	16	10	12	12	13
V. HLS	T	38.5	37	38	38.5	39	38.5	38.5	39	38.5	38	38	39.5	39
	P	136	132	117	121	142	138	125	131	127	127	128	139	139
	R	11	16	18	15	16	14	12	13	13	13	13	13	13
VI. Parkland Formula	T	39	38	39	39.5	39.5	39.5	39.5	39.5	38.5	38.5	38	39	38.5
	P	100	118	124	133	111	153	133	128	124	122	116	139	118
	R	15	17	21	18	15	13	12	11	12	13	13	15	13

TABLE 8. Vital Signs (T = Rectal Temperature, P = Pulse Rate, & R = Pespiratory Rate) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group	Blood Pressure	Time Postburn (Hours) 0	1	2	4	6	8	10	12	18	24	30	36	48
I. Control	Arterial	137/82	138/98	147/106	121/83	128/77	150/97	133/83	135/82	150/110	136/91	97/58	126/94	116/83
	Venous	-5/-20	2/-18	-1/-25	-2/-18	-7/-15	+6/-13	-4/-12	6/-18	-5/-18	1/-10	1/-14	6/-19	4/-14
II. Burn, Non-Resuscitated	Arterial	136/92	157/100	146/93	150/98	123/76	129/79	124/60	110/67	127/79	136/80	114/66	136/90	135/89
	Venous	-1/-12	0/-11	2/-16	-1/-13	3/-15	-5/-19	2/-11	-2/-15	0/-16	0/-13	0/-9	-2/-10	-7/-13
III. "Brooke Formula"	Arterial	157/111	168/102	150/105	140/92	136/87	137/87	143/92	142/93	141/88	139/102	131/88	123/76	127/74
	Venous	-4/-9	13/-17	9/-16	8/-16	8/-16	6/-18	9/-12	6/-15	12/-13	12/-10	23/-17	20/-13	16/-19
IV. Lactated Ringer's	Arterial	145/93	155/105	152/86	138/90	135/90	132/84	142/88	154/90	132/83	128/80	136/84	136/88	146/86
	Venous	-4/-17	-2/-15	-2/-15	-4/-12	0/-7	-1/-8	-2/-6	-2/-7	-3/-12	-4/-14	1/-12	9/-16	5/-12
V. HLS	Arterial	141/101	140/89	170/120	146/101	137/90	130/84	142/99	137/88	140/88	149/88	127/83	138/88	133/90
	Venous	-4/-19	12/-19	3/-22	0/-15	5/-17	4/-21	6/-15	6/-15	4/-12	3/-11	5/-15	7/-13	6/-9
VI. Parkland Formula	Arterial	148/103	190/123	173/111	165/115	168/114	150/100	139/89	156/103	130/79	130/81	118/76	134/82	122/79
	Venous	-3/-15	-3/-17	-5/-19	1/-14	-1/-14	-7/-22	2/-15	-3/-18	5/-14	14/-7	6/-14	4/-11	9/-7

TABLE 9. Arch Aortic and Central Venous Blood Pressures for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group		Time Postburn (Hours) 0	1	2	3	4	5	6	8	10	12	18	24	30	36	48
I.	Control	35	35	36	35	33	34	33	33	32	32	33	30	29	30	29
II.	Burn, Non-Resuscitated	33	34	35	32	32	31	33	32	32	31	31	28	26	23	25
III.	"Brooke Formula"	34	35	33	34	32	31	30	30	27	29	27	26	25	26	25
IV.	Lactated Ringer's	35	35	33	32	32	33	32	32	32	29	29	27	24	26	26
V.	HLS	34	34	34	33	34	34	33	33	33	33	31	28	27	27	27
VI.	Parkland Formula	36	36	35	34	35	35	34	33	31	30	29	27	27	26	27

TABLE 10. Hematocrit Levels (%) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group	Percent of Administered Sodium Load Excreted in Urine		
	First 24 Hours	Second 24 Hours	48 Hours
I. Control	61%	343%	142%
II. Burn, Non-Resuscitated	61%	147%	75%
III. "Brooke Formula"	49%	68%	53%
IV. Lactated Ringer's	55%	97%	68%
V. HLS	24%	113%	53%
VI. Parkland Formula	55%	113%	75%

TABLE 11. Percent of Administered Sodium Load Excreted in the Urine for Each Treatment Group

Treatment Group	Time Postburn (Hours)							
	0	4	8	12	18	24	36	48
I. Control	99	104	104	103	104	102	102	103
II. Burn, Non-Resuscitated	98	100	103	103	104	104	104	106
III. "Brooke Formula"	100	103	105	106	108	108	110	113
IV. Lactated Ringer's	98	99	102	96	103	100	104	104
V. HLS	98	99	103	105	109	110	113	116
VI. Parkland Formula	101	101	105	106	105	104	103	103

TABLE 12. Serum Chloride Values (mEq/L) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group	Time Postburn (Hours) 0	4	8	12	18	24	36	48
I. Control	4.7	4.7	4.6	4.3	4.0	4.2	4.3	3.9
II. Burn, Non-Resuscitated	4.3	4.5	4.3	4.4	3.9	4.4	4.4	3.9
III. "Brooke Formula"	4.7	5.1	4.9	4.3	4.2	4.1	4.1	4.2
IV. Lactated Ringer's	4.2	4.4	4.7	4.2	3.9	3.9	3.9	4.1
V. HLS	4.4	4.5	4.3	4.0	3.9	3.8	4.1	4.9
VI. Parkland Formula	4.1	4.7	4.4	4.3	4.2	4.0	4.1	4.0

TABLE 13. Serum Potassium Determination (mEq/L) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group	Time Postburn (Hours) 0	4	8	12	18	24	36	48
I. Control	8.3	9.2	8.3	8.3	8.2	7.9	8.7	8.0
II. Burn, Non-Resuscitated	8.6	8.4	8.1	7.8	7.8	7.8	7.7	7.5
III. "Brooke Formula"	9.4	9.0	8.8	8.7	9.0	8.9	9.6	9.8
IV. Lactated Ringer's	8.9	8.2	8.1	7.7	7.8	8.1	9.3	7.9
V. HLS	8.9	8.0	7.8	7.1	8.0	7.9	8.1	7.5
VI. Parkland Formula	9.7	8.9	8.6	8.8	8.7	9.1	8.9	9.3

TABLE 14. Serum Calcium Levels (mEq/L) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group		Time Postburn (Hours) 0	4	8	12	18	24	36	48
I.	Control	21	23	21	22	20	23	22	22
II.	Burn, Non-Resuscitated	22	25	25	24	22	25	25	24
III.	"Brooke Formula"	24	23	24	26	25	25	24	24
IV.	Lactated Ringer's	23	24	24	23	24	25	24	24
V.	HLS	23	25	26	27	28	28	28	25
VI.	Parkland Formula	24	25	24	26	26	27	26	26

TABLE 15. Serum Bicarbonate Determinations (mEq/L) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group		Time Postburn (Hours) 0	4	8	12	18	24	36	48
I.	Control	17	8	16	10	33	15	15	5
II.	Burn, Non-Resuscitated	16	15	11	10	9	7	9	11
III.	"Brooke Formula"	23	15	11	6	9	13	8	8
IV.	Lactated Ringer's	25	27	4	22	17	13	4	15
V.	HLS	20	26	17	11	15	35	13	10
VI.	Parkland Formula	9	4	10	4	5	5	7	5

TABLE 16. Lactate Values (mg/100 ml) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group		Time Postburn (Hours) 0	4	8	12	18	24	36	48
I.	Control	122*	127	133	1[illegible]	153	133	131	131
II.	Burn, Non-Resuscitated	101	128	142	153	113	103	93	86
III.	"Brooke Formula"	123*	120	84	85	78	68	73	74
IV.	Lactated Ringer's	151*	121	103	96	99	85	82	89
V.	HLS	128*	117	129	121	119	126	100	96
VI.	Parkland Formula	91	92	79	86	82	78	72	78

TABLE 17. Blood Glucose Determinations (mg/100 ml) for Each Treatment Group for the Initial 48 Hour Intensive Care Period. (*Groups Having One Diabetic Animal included.)

Treatment Group		Time Postburn (Hours) 0	4	8	12	18	24	36	48
I.	Control	6.3	6.6	7.4	7.7	7.0	6.3	6.4	6.1
II.	Burn, Non-Resuscitated	6.9	6.4	6.2	6.2	5.9	5.8	7.1	7.1
III.	"Brooke Formula"	8.3	8.2	7.7	6.5	7.4	6.0	7.5	6.7
IV.	Lact[illegible]ted Ringer's	7.2	6.9	6.4	6.1	6.8	6.1	6.3	6.4
V.	HLS	8.2	7.9	6.7	8.1	8.0	7.0	6.9	7.0
VI.	Parkland Formula	6.7	7.1	5.1	5.2	5.1	5.1	7.2	5.9

TABLE 18. Protein Determinations (g/100 ml) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group		Time Postburn (Hours) 0	4	8	12	18	24	36	48
I.	Control	15	17	18	17	15	13	11	11
II.	Burn, Non-Resuscitated	16	22	23	23	24	25	27	28
III.	"Brooke Formula"	19	19	19	14	17	19	16	17
IV.	Lactated Ringer's	18	19	17	15	15	13	13	13
V.	HLS	20	24	24	22	22	21	19	21
VI.	Parkland Formula	19	19	17	16	14	13	11	11

TABLE 19. Blood Area Nitrogen (BUN) (mg/100 ml) Values for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group		Time Postburn (Hours) 0	4	8	12	18	24	36	48
I.	Control	1.2	1.1	1.1	1.2	1.1	1.0	1.1	1.1
II.	Burn, Non-Resuscitated	1.1	1.1	1.1	1.3	1.1	1.1	1.2	1.1
III.	"Brooke Formula"	1.2	1.3	1.4	1.0	1.2	1.2	1.2	1.0
IV.	Lactated Ringer's	1.4	1.3	1.2	1.2	1.1	1.1	1.1	1.1
V.	HLS	1.4	1.4	1.3	1.3	1.3	1.3	1.2	1.4
VI.	Parkland Formula	1.5	1.4	1.3	1.3	1.2	1.1	1.1	1.0

TABLE 20. Serum Creatinine Levels (mg/100 ml) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group	Time Postburn (Hours) 0	1	4	8	12	18	24	36	48
I. Control	165	232	207	237	263	258	233	206	188
II. Burn, Non-Resuscitated	46	117	170	163	181	209	254	264	270
III. "Brooke Formula"	62	140	110	77	72	60	60	99	152
IV. Lactated Ringer's	103	160	177	137	142	95	65	95	96
V. HLS	83	168	106	162	178	199	183	142	189
VI. Parkland Formula	179	183	131	114	114	47	42	59	47

TABLE 21. Urine Creatinine Values (mg/100 ml) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group	Time Postburn (Hours) 0	1	4	8	12	18	24	36	48
I. Control	321	312	334	303	305	292	292	297	339
II. Burn, Non-Resuscitated	299	295	321	299	302	290	383	296	296
III. "Brooke Formula"	300	323	342	312	327	304	322	325	306
IV. Lactated Ringer's	304	357	313	328	311	308	295	305	303
V. HLS	298	289	313	305	309	318	319	317	332
VI. Parkland Formula	288	299	320	302	305	323	323	312	298

TABLE 22. Serum Osmolarity Determinations (mOsm/L) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

	Treatment Group	Time Postburn (Hours) 0	1	4	8	12	18	24	36	48
I.	Control	730	893	953	1010	939	1115	901	859	913
II.	Burn, Non-Resuscitated	455	690	821	1221	833	984	952	941	911
III.	"Brooke Formula"	414	617	699	766	740	644	808	946	1039
IV.	Lactated Ringer's	673	790	816	874	855	690	645	740	707
V.	HLS	609	777	910	944	1001	966	987	922	954
VI.	Parkland Formula	495	762	735	732	661	729	547	482	539

TABLE 23. Urinary Osmolarity Values (mOsm/L) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group	Arterial Blood Gases	Time Postburn (Hours) 0	1	2	4	6	8	12	18	24	36	48
I. Control	pH	7.54	7.59	7.58	7.58	7.59	7.60	7.56	7.57	7.56	7.60	7.58
	pO_2	87	67	65	68	68	83	75	87	81	82	74
	pCO_2	35	33	32	21	23	23	34	26	25	28	36
II. Burn, Non-Resuscitated	pH	7.55	7.56	7.59	7.56	7.56	7.56	7.52	7.58	7.58	7.57	7.56
	pO_2	78	59	71	71	70	68	69	78	76	56	60
	pCO_2	27	41	37	34	29	31	30	21	22	22	24
III. "Brooke Formula"	pH	7.56	7.61	7.62	7.56	7.57	7.56	7.54	7.42	7.40	7.61	7.62
	pO_2	67	54	61	62	47	72	71	80	64	71	66
	pCO_2	26	33	28	27	24	26	29	37	48	21	26
IV. Lactated Ringer's	pH	7.55	7.55	7.55	7.57	7.58	7.57	7.57	7.60	7.58	7.60	7.57
	pO_2	73	74	61	63	60	68	61	61	65	57	56
	pCO_2	33	34	41	41	40	34	--	45	42	36	45
V. HLS	pH	7.57	7.52	7.55	7.60	7.58	7.62	7.62	7.62	7.57	7.57	7.59
	pO_2	76	79	79	78	75	69	75	66	70	61	66
	pCO_2	38	26	27	24	24	35	35	43	40	43	42
VI. Parkland Formula	pH	7.56	7.54	7.61	7.58	7.58	7.56	7.65	7.62	7.63	7.60	7.61
	pO_2	51	53	35	59	64	61	60	71	73	68	69
	pCO_2	43	40	41	31	25	26	25	25	63	28	33

TABLE 24. Arterial Blood Gases (pH and P in mm Hg) for Each Treatment Group for the Initial 48 Hour Intensive Care Period

Treatment Group		Time Postburn (Hours) 0	1	4	8	12	18	24	36	48
I.	Control	1.022	1.023	1.027	1.030	1.030	1.029	1.031	1.024	1.023
II.	Burn, Non-Resuscitated	1.011	1.024	1.024	1.028	1.028	1.020	1.026	1.024	1.021
III.	"Brooke Formula"	1.012	1.024	1.021	1.020	1.021	1.021	1.019	1.025	1.030
IV.	Lactated Ringer's	1.017	1.024	1.020	1.026	1.024	1.018	1.015	1.018	1.021
V.	HLS	1.016	1.025	1.028	1.026	1.031	1.034	1.031	1.030	1.025
VI.	Parkland Formula	1.018	1.030	1.017	1.017	1.017	1.015	1.015	1.016	1.013

TABLE 25. Urine Specific Gravity for Each Treatment Group for the Initial 48 Hour Intensive Care Period